

**PENDING CLAIMS AS AMENDED****(MARKED UP VERSION)**

WE CLAIM:

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1. (withdrawn) A medical system for treating a neurodegenerative disorder comprising:
 - a. an intracranial access device;
 - b. a mapping means for locating a predetermined location in the brain;
 - c. a deliverable amount of a small interfering RNA or vector encoding said small interfering RNA; and
 - d. a delivery means for delivering said small interfering RNA or vector encoding said small interfering RNA to said location of the brain from said intracranial access device.

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2. (withdrawn) A medical system of claim 1 wherein said neurodegenerative disorder is Parkinson's disease.

3. (withdrawn) A medical system of claim 1 wherein said neurodegenerative disorder is Alzheimer's disease.

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4. (withdrawn) A medical system of claim 1 wherein said neurodegenerative disorder is Huntington's disease.

5. (original) A medical system of claim 1 wherein said neurodegenerative disorder is spinocerebellar ataxia type 1.

6. (withdrawn) A medical system of claim 1 wherein said neurodegenerative disorder is spinocerebellar ataxia type 2.

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7. (withdrawn) A medical system of claim 1 wherein said neurodegenerative disorder is spinocerebellar ataxia type 3, also known as Machado-Joseph disease.

8. (withdrawn) A medical system of claim 1 wherein said neurodegenerative disorder is dentatorubral-pallidoluysian atrophy, also known as DRPLA.

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9. (original) A medical system of claim 1 wherein said intracranial access device is an intracranial catheter.

10. (original) A medical system of claim 1 wherein said intracranial access device is an intracranial access port.

11. (original) A medical system of claim 1 wherein said predetermined location is the substantia nigra.

12. (original) A medical system of claim 1 wherein said predetermined location is the nucleus basalis of Meynert or the cerebral cortex.
13. (original) A medical system of claim 1, wherein said predetermined location is the caudate nucleus, the putamen, or the striatum.
- 5 14. (original) A medical system of claim 1 wherein said predetermined location is the dentate nucleus, emboliform nucleus, the globose nucleus, the fastigial nucleus of the cerebellum (collectively the deep cerebellar nuclei), or the cerebellar cortex.
15. (original) A medical system of claim 1 wherein said predetermined location is the subthalamic nucleus.
- 10 16. (original) A medical system of claim 1 wherein said small interfering RNA is complementary to the mRNA for alpha-synuclein.
17. (original) A medical system of claim 1 wherein said small interfering RNA is complementary to the mRNA for beta amyloid cleaving enzyme type 1, or BACE1.
18. (original) A medical system of claim 1 wherein said small interfering RNA is
15 complementary to the mRNA transcript from the IT15 gene, including the code for the huntingtin protein.
19. (original) A medical system of claim 1 wherein said small interfering RNA is complementary to the mRNA transcript from the SCA1 gene, including the code for the ataxin1 protein.
- 20 20. (original) A medical system of claim 1 wherein said small interfering RNA is complementary to the mRNA transcript from the SCA2 gene, including the code for the ataxin2 protein.
21. (original) A medical system of claim 1 wherein said small interfering RNA is complementary to the mRNA transcript from the SCA3 gene, including the code for
25 the ataxin3 protein, also known as the Machado-Joseph protein.
22. (original) A medical system of claim 1 wherein said small interfering RNA is complementary to the mRNA transcript from the DRLPA gene, including the code for the atrophin1 protein.
23. (original) A medical system of claim 1 wherein said small interfering RNA is
30 substantially provided for in any one of **SEQ ID Nos: 1-44**.
24. (original) A medical system of claim 1 wherein said delivery means is injection from an external syringe into an intracranial access port.

25. (original) A medical system of claim 1 wherein said delivery means is an infusion pump.

26. (withdrawn) An infusion pump of claim 25 wherein the said infusion pump is an electromechanical pump.

5 27. (withdrawn) An infusion pump of claim 25 wherein the said infusion pump is an osmotic pump.

28. (withdrawn) A method for treating a neurodegenerative disorder comprised of modulating the expression or production of a protein in neurons by intracranial delivery of a small interfering RNA that reduces said expression or production of said protein, in a pharmaceutically acceptable carrier.

10 29. (withdrawn) A method of delivering a small interfering RNA to a location in the brain comprising the steps of:

- a. surgically implanting an intracranial access delivery device; and
- b. infusing a small interfering RNA and/or a vector encoding said small interfering RNA at a predetermined site in the brain.

15 30. (withdrawn) A method of delivering a small interfering RNA to a location in the brain comprising the steps of:

- a. surgically implanting an intracranial access delivery device; and
- b. infusing a small interfering RNA and/or a vector encoding said small interfering RNA at a predetermined site in the brain; wherein at least one attribute of said neurodegenerative diseases is reduced or its progression slowed or arrested.

20 31. (withdrawn) The method of claim 30, wherein said step of implanting the catheter is performed after said neurodegenerative disorder is diagnosed.

25 32. (withdrawn) The method of claim 31, wherein said step of implanting the catheter is performed after said neurodegenerative disorder is diagnosed and before the symptoms of the said neurodegenerative disorder are manifest.

30 33. (withdrawn) The method of claim 31, wherein said step of implanting the catheter is performed after said neurodegenerative disorder is diagnosed and after the symptoms of the said neurodegenerative disorder are manifest.

34. (withdrawn) The method of any one of claims 29, 30, or 31, wherein said intracranial access delivery device is an intracranial access port coupled to the proximal end of an intracranial catheter.

35. (withdrawn) The method of any one of claims 29, 30, or 31, further comprising the steps of: implanting a pump outside the brain, the pump coupled to the proximal end of an intracranial catheter.
- 5 36. (withdrawn) The method of claim 35 comprising operating the pump to deliver a predetermined dosage of the said small interfering RNA or vector encoding said small interfering RNA from the pump through the discharge portion of the said intracranial catheter.
37. (withdrawn) The method of claim 35 further comprising the step of periodically refreshing the pump with at least one substance.
- 10 38. (withdrawn) The method of claim 35 wherein said pump is an infusion pump.
39. (withdrawn) The method of claim 38 wherein said infusion pump is an electromechanical pump.
40. (withdrawn) The method of claim 38 wherein said infusion pump is an osmotic pump.
41. (withdrawn) A method of claims 28 or 30, wherein said neurodegenerative disorder is
15 Parkinson's disease.
42. (withdrawn) A method of claims 28 or 30 wherein said neurodegenerative disorder is Alzheimer's disease.
43. (withdrawn) A method of claims 28 or 30, wherein said neurodegenerative disorder is Huntington's disease.
- 20 44. (withdrawn) A method of claims 28, or 30 wherein said neurodegenerative disorder is spinocerebellar ataxia type 1.
45. (withdrawn) A method of claims 28 or 30, wherein said neurodegenerative disorder is spinocerebellar ataxia type 2.
46. (withdrawn) A method of claims 28 or 30, wherein said neurodegenerative disorder is
25 spinocerebellar ataxia type 3, also known as Machado-Joseph disease.
47. (withdrawn) A method of claims 28 or 30, wherein said neurodegenerative disorder is dentatorubral-pallidoluysian atrophy, also known as DRPLA.
48. (withdrawn) A method of claims 29 or 30, wherein the said predetermined site in the brain is the substantia nigra.
- 30 49. (withdrawn) A method of claims 29 or 30, wherein the said predetermined site in the brain is the nucleus basalis of Meynert or the cerebral cortex.
50. (withdrawn) A method of claims 29 or 30, wherein the said predetermined site in the brain is the caudate nucleus, the putamen, or the striatum.

51. (withdrawn) A method of claims 29 or 30, wherein the said predetermined site in the brain is the dentate nucleus, emboliform nucleus, the globose nucleus, the fastigial nucleus of the cerebellum (collectively the deep cerebellar nuclei), or the cerebellar cortex.
- 5 52. (withdrawn) A method of claims 29 or 30, wherein the said predetermined site in the brain is the subthalamic nucleus.
53. (withdrawn) A method of claims 28, 29, or 30, wherein said small interfering RNA is complementary to the mRNA for alpha-synuclein.
- 10 54. (withdrawn) A method of claims 28, 29, or 30 wherein said small interfering RNA is complementary to the mRNA for beta amyloid cleaving enzyme type 1, or BACE1.
55. (withdrawn) A method of claims 28, 29 or 30 wherein said small interfering RNA is complementary to the mRNA transcript from the IT15 gene, including the code for the huntingtin protein.
- 15 56. (withdrawn) A method of claims 28, 29, or 30 wherein said small interfering RNA is complementary to the mRNA transcript from the SCA1 gene, including the code for the ataxin1 protein.
57. (withdrawn) A method of claims 28, 29, or 30 wherein said small interfering RNA is complementary to the mRNA transcript from the SCA2 gene, including the code for the ataxin2 protein.
- 20 58. (withdrawn) A method of claims 28, 29, or 30 wherein said small interfering RNA is complementary to the mRNA transcript from the SCA3 gene, including the code for the ataxin3 protein, also known as the Machado-Joseph protein.
59. (withdrawn) A method of claims 28, 29 or 30 wherein said small interfering RNA is complementary to the mRNA transcript from the DRLPA gene, including the code for the atrophin1 protein.
- 25 60. (withdrawn) A method of claims 28, 29, or 30 wherein said small interfering RNA is delivered by a delivery vector.
61. (withdrawn) A method of claim 60 wherein the delivery vector is adeno-associated virus, or AAV.
- 30 62. (withdrawn) A method of claim 60 wherein the delivery vector is adenovirus.
63. (withdrawn) A method of claim 60 wherein the delivery vector is herpes simplex virus, or HSV.
64. (withdrawn) A method of claim 60 wherein the delivery vector is lentivirus.

65. (withdrawn) A method of claim 60 wherein the delivery vector is a DNA plasmid.
66. (withdrawn) A method of claim 65 wherein the said DNA plasmid is complexed with a liposomal compound.
67. (withdrawn) A method of claim 65 wherein the said DNA plasmid is complexed with polyethylenimine (PEI).
68. (withdrawn) A small interfering RNA containing sequences according to **SEQ ID Nos 1-4**-, or a partial sequence thereof, or a base sequence hybridizable to a complementary strand of RNA encoding a protein associated with a neurodegenerative disease.
69. (withdrawn) A small interfering RNA comprising an RNA sequence hybridizable to the RNA sequence encoding a protein associated with a neurodegenerative disease to cause cleavage of said protein-encoding RNA sequence.
70. (withdrawn) A small interfering RNA expression sequence comprising the DNA sequence encoding an RNA sequence hybridizable to the RNA sequence encoding a protein associated with a neurodegenerative disease to cause cleavage of said protein-encoding RNA sequence.
71. (withdrawn) A small interfering RNA of any of claims 68, 69, or 70 wherein said neurodegenerative disease is Parkinson's disease.
72. (withdrawn) A small interfering RNA of any of claims 68, 69, or 70 wherein said neurodegenerative disease is Alzheimer's disease.
73. (withdrawn) A small interfering RNA of any of claims 68, 69, or 70 wherein said neurodegenerative disease is Huntington's disease.
74. (withdrawn) A small interfering RNA of any of claims 68, 69, or 70 wherein said neurodegenerative disease is spinocerebellar ataxia type 1.
75. (withdrawn) A small interfering RNA of any of claims 68, 69, or 70 wherein said neurodegenerative disease is spinocerebellar ataxia type 2.
76. (withdrawn) A small interfering RNA of any of claims 68, 69, or 70 wherein said neurodegenerative disease is spinocerebellar ataxia type 3, also known as Machado-Joseph disease.
77. (withdrawn) A small interfering RNA of any of claims 68, 69, or 70 wherein said neurodegenerative is dentatorubral-pallidoluysian atrophy, also known as DRPLA.
78. (withdrawn) A small interfering RNA of any of claims 68, 69, or 70 wherein said small interfering RNA is complementary to the mRNA for alpha-synuclein.

79. (withdrawn) A small interfering RNA of any of claims 68, 69, or 70 wherein said small interfering RNA is complementary to the mRNA for beta amyloid cleaving enzyme type 1, or BACE1.
- 5 80. (withdrawn) A small interfering RNA of any of claims 68, 69, or 70 wherein said small interfering RNA is complementary to the mRNA transcript from the IT15 gene, including the code for the huntingtin protein.
81. (withdrawn) A small interfering RNA of any of claims 68, 69, or 70 wherein said small interfering RNA is complementary to the mRNA transcript from the SCA1 gene, including the code for the ataxin1 protein.
- 10 82. (withdrawn) A small interfering RNA of any of claims 68, 69, or 70 wherein said small interfering RNA is complementary to the mRNA transcript from the SCA2 gene, including the code for the ataxin2 protein.
83. (withdrawn) A small interfering RNA of any of claims 68, 69, or 70 wherein said small interfering RNA is complementary to the mRNA transcript from the SCA3 gene, including the code for the ataxin3 protein, also known as the Machado-Joseph protein.
- 15 84. (withdrawn) A small interfering RNA of any of claims 68, 69, or 70 wherein said small interfering RNA is complementary to the mRNA transcript from the DRLPA gene, including the code for the atrophin1 protein.